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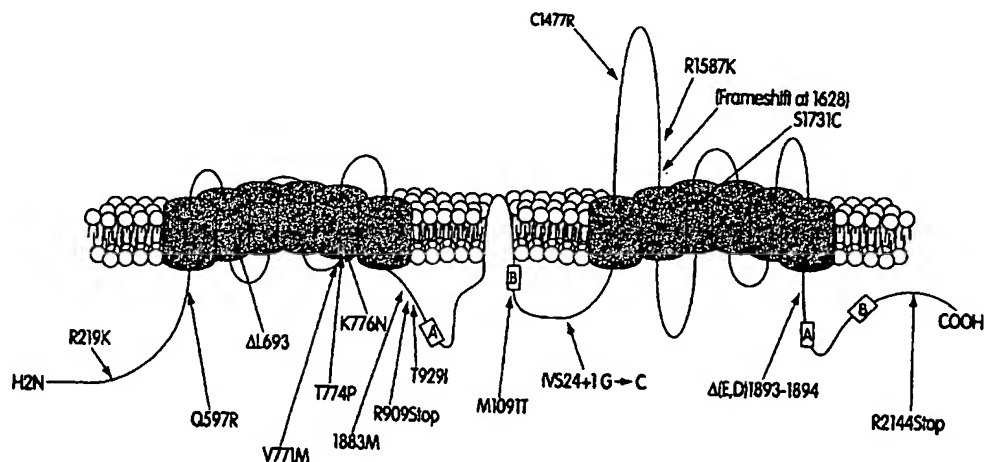
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[Continued on next page]

(54) Title: ABC1 POLYPEPTIDE AND METHODS AND REAGENTS FOR MODULATING CHOLESTEROL LEVELS



(57) Abstract: The invention features ABC1 nucleic acids and polypeptides for the diagnosis and treatment of abnormal cholesterol regulation. The invention also features methods for identifying compounds for modulating cholesterol levels in an animal (e.g., a human).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

- (15) Information about Correction:**
see PCT Gazette No. 28/2001 of 12 July 2001, Section II

INTERNATIONAL SEARCH REPORT

International Application No

PC1/IB 00/00532

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/705 C12N5/10 A01K67/027 C12N15/00
A61K38/17 A61K48/00 A61K38/45 A61K31/00 A61K31/70
G01N33/68 C12Q1/68 C12N15/11

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, STRAND, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LUCIANI M F ET AL: "CLONING OF TWO NOVEL ABC TRANSPORTERS MAPPING ON HUMAN CHROMOSOME 9" GENOMICS,US,ACADEMIC PRESS, SAN DIEGO, vol. 21, no. 1, 1 May 1994 (1994-05-01), pages 150-159, XP000869719 ISSN: 0888-7543	1,2,9, 10, 14-16, 33-36, 38, 49-51, 72,73, 80,81
Y	the whole document	23,27, 32,37, 39-46, 67-71, 74-79

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

23 October 2000

Date of mailing of the international search report

08. 11. 00

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PC/IB 00/00532

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EMBL/GENBANK DATABASE Accession no AJ012376 Sequence ID HSA012376 7 January 1999 LANGMANN T ET AL: "Molecular cloning of the human ATP-binding cassette transporter 1 (hABC1)..." XP002144900	1,2,9, 10, 14-16, 33-36, 38, 49-51, 72,73, 80,81
Y	the whole document	23,27, 32,37, 39-46, 67-71, 74-79
P,X	--- LANGMANN T ET AL: "MOLECULAR CLONING OF THE HUMAN ATP-BINDING CASSETTE TRANSPORTER 1 (hABC1): EVIDENCE FOR STEROL-DEPENDENT REGULATION IN MACROPHAGES" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS,US,ACADEMIC PRESS INC. ORLANDO, FL, vol. 257, no. 1, 2 April 1999 (1999-04-02), pages 29-33, XP000877240 ISSN: 0006-291X	1,2,9, 10,14, 16, 33-36, 38, 49-51, 72,73, 80,81
Y	the whole document	23,27, 32,37, 39-46, 67-71, 74-79
Y	--- RUST S ET AL: "ASSIGNMENT OF TANGIER DISEASE TO CHROMOSOME 9Q31 BY A GRAPHICAL LINKAGE EXCLUSION STRATEGY" NATURE GENETICS,US,NEW YORK, NY, vol. 20, no. 1, September 1998 (1998-09), pages 96-98, XP000884511 ISSN: 1061-4036 the whole document	23,27, 32,37, 39-46, 67-71, 74-79
A	--- BECQ FREDERIC ET AL: "ABC1, an ATP binding cassette transporter required for phagocytosis of apoptotic cells, generates a regulated anion flux after expression in Xenopus laevis oocytes." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 272, no. 5, 1997, pages 2695-2699, XP002150648 ISSN: 0021-9258 --- -/--	

INTERNATIONAL SEARCH REPORT

International Application No

PC1/IB 00/00532

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LUCIANI MARIE-FRANCOISE ET AL: "The ATP binding cassette transporter ABC1, is required for the engulfment of corpses generated by apoptotic cell death." EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 15, no. 2, 1996, pages 226-235, XP002150649 ISSN: 0261-4189 ---	
E	WO 00 18912 A (BAYER AG ;KLUCKEN JOCHEN (DE); SCHMITZ GERD (DE)) 6 April 2000 (2000-04-06) the whole document ---	1,2,9, 10, 14-16, 23, 25-27, 29-42, 44,67-71
P,X	RUST S ET AL: "TANGIER DISEASE IS CAUSED BY MUTATIONS IN THE GENE ENCODING ATP--BINDING CASSETTE TRANSPORTER 1" NATURE GENETICS,US,NEW YORK, NY, vol. 22, no. 4, August 1999 (1999-08), pages 352-355, XP000884993 ISSN: 1061-4036 the whole document ---	1,2,9, 10, 14-16, 23,27, 32-42, 67-73, 75-77,79
P,X	EMBL/GENBANK DATABASE Accession no AF165281 Sequence ID AF165281 17 August 1999 RUST S ET AL:"Tangier disease is caused by mutations in the gene....." XP002144901 the whole document ---	1,2,9, 10,14-16
P,X	REMALEY A T ET AL: "HUMAN ATP-BINDING CASSETTE TRANSPORTER 1 (ABC1): GENOMIC ORGANIZATION AND IDENTIFICATION OF THE GENETIC DEFECT IN THE ORIGINAL TANGIER DISEASE KINDRED" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA,US,NATIONAL ACADEMY OF SCIENCE. WASHINGTON, vol. 96, no. 22, 26 October 1999 (1999-10-26), pages 12685-12690, XP000877247 ISSN: 0027-8424 the whole document ---	1,2,9, 10, 14-16, 23,27, 32-42, 67-73, 75-77,79

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INTERNATIONAL SEARCH REPORT

International Application No

PC/1B 00/00532

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	BODZIOCH MAREK ET AL: "The gene encoding ATP-binding cassette transporter 1 is mutated in Tangier disease." NATURE GENETICS, vol. 22, no. 4, August 1999 (1999-08), pages 347-351, XP002150650 ISSN: 1061-4036 the whole document	1,2,9, 10, 14-16, 23,27, 32-42, 67-73, 75-77,79
P,X	--- BROOKS-WILSON A ET AL: "MUTATIONS IN ABC1 IN TANGIER DISEASE AND FAMILIAL HIGH-DENSITY LIPOPROTEIN DEFICIENCY" NATURE GENETICS,US,NEW YORK, NY, vol. 22, no. 4, August 1999 (1999-08), pages 336-345, XP000889767 ISSN: 1061-4036 the whole document	1,2,9, 10, 14-16, 23,27, 32-42, 67-73, 75-77,79
A	--- HAMON YANNICK ET AL: "Interleukin-1-beta secretion is impaired by inhibitors of the Atp binding cassette transporter, ABC1." BLOOD, vol. 90, no. 8, 1997, pages 2911-2915, XP002150651 ISSN: 0006-4971 the whole document	41-44
X	--- DATABASE MEDLINE [Online] US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; KIM-SCHULZE S ET AL: "Estrogen stimulates delayed mitogen-activated protein kinase activity in human endothelial cells via an autocrine loop that involves basic fibroblast growth factor." retrieved from STN Database accession no. 1998377893 XP002150652	41-44
Y	abstract & CIRCULATION, (1998 AUG 4) 98 (5) 413-21.,	41-44
X	--- DATABASE MEDLINE [Online] US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; HANSEN P S: "Familial defective apolipoprotein B-100." retrieved from STN Database accession no. 1998450452 XP002150653	41-44
Y	abstract & DANISH MEDICAL BULLETIN, (1998 SEP) 45 (4) 370-82. REF: 139,	41,44
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 00/00532

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE MEDLINE [Online] US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; BELLOSTA S ET AL: "Direct vascular effects of HMG- CoA reductase inhibitors." retrieved from STN Database accession no. 1998357922 XP002150654	41-44
Y	abstract & ATHEROSCLEROSIS, (1998 APR) 137 SUPPL S101-9. REF: 66,	41-44
A	--- DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1994 SCHREYER SANDRA A ET AL: "Hypercatabolism of lipoprotein-free apolipoprotein A-I in HDL-deficient mutant chickens." Database accession no. PREV199598077611 XP002150728 abstract & ARTERIOSCLEROSIS AND THROMBOSIS, vol. 14, no. 12, 1994, pages 2053-2059, ISSN: 1049-8834 -----	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 00/00532

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-22 24 28 47 48 52-56 63 66 79 85 completely 23
25-27 29-40 45 46 57-62 64 65 67-74 82-84 86
partially

ABC1 polypeptide with amino acid sequence SEQ ID NO 1
encoded by SEQ ID NO 2 and their uses

2. Claims: 23 25-27 29-40 partially

Use of ABC1 polypeptides or its encoding polynucleotides not
being SEQ ID NO 1 or 2 as pharmaceutical

3. Claims: 41-44 78

Use of compounds that modulates the biological activity of
ABC1 as pharmaceutical

4. Claims: 45 46 57-62 64 65 72-74 82-84 86 partially

Use of ABC1 polypeptides or their encoding nucleotides not
being SEQ ID NO 1 or 2 in assays

5. Claims: 49-51 80 81

Nucleic acid comprising a region at least 80% identical to at
least 30 contiguous nucleotides of SEQ ID NO 14 and their
use.

6. Claims: 67-71 75-77

Methods for determining a person's properties related to the
ABC1 gene or activity

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 23-44 78 are (partially) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Although claims 45-46 61 62 and 67-71 75-77 are (partially) directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 00/00532

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0018912 A	06-04-2000	AU 5980499 A	17-04-2000